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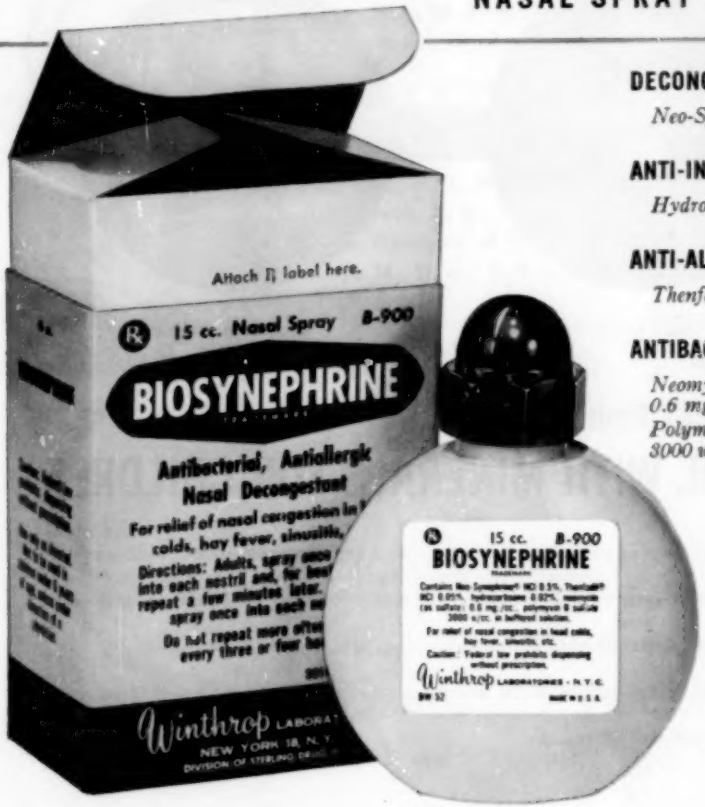

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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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E D I T O R I A L

NEW PRODUCTS AND THE FREE ENTERPRISE SYSTEM

PHARMACISTS are often highly critical of the continuing deluge of new prescription products which descend upon them year after year. This does cause many problems at the retail level, as everyone can well imagine. The question that must be resolved is whether the over-all and net effect is good or bad—to the pharmacist, to the industry as a whole, and to society. There is also the question whether any one part of the present system, considered bad, could be altered without altering or destroying those aspects which are good.

New products are the lifeblood of the pharmaceutical industry. Companies which fail to develop and promote them soon are left behind and suffer economic pressures threatening them with extinction. The successful company spends much of its income in supporting research and in promotional efforts to exploit the results of this research. Thus, the most striking examples of rapid growth in the pharmaceutical industry have been those companies which follow this policy.

Such highly competitive effort has been the source of most of today's miracle drugs. These same miracle drugs have been largely responsible for raising life-expectancy over five years in the last two decades. They, too, are the basis of the resurgence of pharmacy and its ever increasing importance and recognition by both the public and the medical profession.

As every recent study has shown, it is these prescription specialties which are the chief source of profit in the successful pharmacy today. In fact, the economic health of any retail pharmacy is best measured by its prescription volume. Thus, the unprecedented physical and financial growth of the pharmaceutical industry has extended into every facet of pharmacy including retail pharmacy and new prescription products are the *sine qua non* of the entire picture.

It is a characteristic of human nature that man always prefers roses without thorns and would like to enjoy the sweet without the slightest taste of the bitter. This is the difficulty with prescription specialties. It would be nice to have just the profit that these bring without the necessity of a high inventory and the problem of "dead" items draining off some of the return from fast moving products, but such cannot be.

One frequently hears the comment that "there ought to be a law" restraining manufacturers in their overenthusiastic efforts. There is one—an economic law. When a poorly conceived and unnecessary product is released, the manufacturer pays dearly for his error. Any other sort of law, such as federal legislation, would mean the destruction of free enterprise. Before we blithely propose this, we should consider very carefully its full implications. Might this not destroy all the initiative and effort which has made us the most advanced nation in the world in our medicinal wonders? Furthermore, would pharmacists favor restricting the number of pharmacies on a quota system? This is a part of government regulation and interference with free enterprise and is practiced in many countries. Here, any pharmacist can open a store wherever he pleases and have an inventory as high or low as he chooses. So is it also with the manufacturer—he can place on the market that which he feels may bring him profit. Both are free to succeed or fail in the exercise of their own judgment. This is a part of our economic system and it cannot be altered just in part.

It is true, of course, that the manufacturer does have an obligation to be concerned with the problems of the retailer since, if any part of the body of pharmacy should sicken, it affects the whole organism. By and large, reputable manufacturers are concerned and interested in retailers and are showing more concern over their economic problems today than ever before.

In assuming the presidency of the National Pharmaceutical Council recently, Mr. Carl K. Raiser in his address made this important and timely statement:

> "I think that we, as manufacturers, who are so eager to have the pharmacist understand *our* problems, are also under obligation to understand *his* problems, as well. . . . For many an overworked pharmacist, the steady stream of new products and the multiplication of dosage forms, while worthwhile and necessary, nevertheless sometimes assume the proportion of a Johnstown Flood."

We commend Mr. Raiser for his frank and honest appraisal of this problem. It is this sort of pharmaceutical statesmanship which is greatly needed today to bring better understanding and cooperation among all segments of pharmacy.

L. F. Tice

NEW DRUGS OF 1957

By L. F. Tice *

The modern pharmacist must keep abreast of the constant changes taking place in medicinal agents. As today's specialist on the selection and use of drugs, he must know what is new and how new drugs compare with older and well established drugs. He must also keep a constant check on their clinical success and acceptance as experience is gained with them. It is this knowledge and service to the medical profession which continues to fortify pharmacy's position on the health team.

Analgesics

THE development of synthetic analgesics related to morphine, meperidine, and methadone continues. A recently developed drug having useful analgesic properties is d-propoxyphene hydrochloride (Darvon-Lilly). This chemically is α-d-4-dimethylamino-1,2-diphenyl-3-methyl-2-propionoxybutane hydrochloride. In its structure, it is closely related to methadone but the latter is a ketone while Darvon is an ester.

Darvon has about the same analgetic potency as codeine but lacks many of its disadvantages. It is non-narcotic, does not produce euphoria or a dependence on the drug, and is not constipating. Its dose is 32 mg. every 4 hours or 65 mg. three or four times daily. Like codeine, it is often given with other analgesics which potentiate it. In addition to capsules of the drug itself, a combination with acetophenetidin, aspirin, and caffeine is supplied as Pulvules Darvon Compound. Darvon is useful in such painful conditions as arthritis, neuralgias, myositis, pain of traumatic origin, headache, and migraine.

A new drug closely related structurally to meperidine is Ethoheptazine which is used as the citrate. It is also known as Wy 401 which was its Wyeth experimental number. Chemically, this is identical to meperidine except that the six-membered saturated ring

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piperidine in meperidine is replaced by a seven-membered nitrogen containing saturated ring. The chemical name of Ethoheptazine citrate is 1-methyl-4-carbethoxy-4-phenyl hexamethylenimine citrate. It is claimed to be equal to or superior to codeine and non-addicting. Wyeth has released it in combination with acetylsalicylic acid as Zactirin Tablets. These contain 75 mg. of Ethoheptazine with 325 mg. of acetylsalicylic acid.

The morphine antagonist, Nalorphine, is known to have analgesic properties if given in adequate doses. At such high dosage levels, its side effects limit its usefulness. This demonstrates, however, that analgesic action and addicting properties are not necessarily associated. A lower homologue of morphine, normorphine, has given considerable evidence of being a useful and yet a safer analgesic than morphine. Normorphine must be given in larger doses than morphine but it causes much fewer side reactions, such as respiratory depression, and does not appear to be as strongly addicting. It also promises to be useful in treating morphine addicts. It will maintain them adequately when it is substituted for morphine but then, when it is withdrawn, it does not cause as severe a distress as the direct withdrawal of morphine itself.

A new analgesic chemically related to meperidine is the drug Anileridine Phosphate (Leritine—Merck Sharp & Dohme). Anileridine is the 4-aminophenmethyl derivative of meperidine and its pharmacological properties are somewhat similar. Thus, it has good spasmolytic activity unlike morphine and does not produce as much respiratory depression and nausea. It is a more potent drug than meperidine and is of value as preanesthetic medication during anethesia and also as an analgesic in various painful conditions. For oral use, it is prepared in 25 mg. tablets as the dihydrochloride. For injection purposes, it is supplied as the phosphate in ampuls and vials containing 25 mg./cc. Overdosage or respiratory depression following its use can be controlled by the use of Nalorphine given in 1/20th. the dose of Anileridine taken.

Anti-Epileptics

The list of drugs useful in epilepsy continues to grow. Two new drugs in this category are Methsuximide (Celontin—Parke-Davis) and Ethotoin (Peganone—Abbott). Methsuximide is N-methyl-2,2-phenylmethylsuccinimide. It differs from the drug Milontin

(Parke-Davis) only in having an additional methyl at position 2 on the succinimide ring. It is useful in petit mal epilepsy and psychomotor seizures.

Ethotoin is 5-phenyl-3-ethyl hydantoin and, as such, is a close relative of diphenylhydantoin. It is employed in grand mal elipepsy and psychomotor seizures. In mixed types of epilepsy, it can be used with other anti-epileptic drugs.

Antihistamines

Antihistamines are still widely employed in medicine but the release of new drugs in this category has declined. Some drugs once classified as antihistamines have been redirected and reclassified as ataractics (tranquilizers). Such was the case with the antihistamine Phenyltoloxamine, formerly sold as Bristamin (Bristol Laboratories). It is now recommended as a tranquilizer under the name PRN and distributed chiefly to mental hospitals and other institutions.

Most antihistamines produce various degrees of drowsiness as a side effect. One notable exception is the drug Phenindamine Tartrate (Roche) which has been used extensively for several years. A new antihistamine, Isothiphendyl hydrochloride (Theruhistin—Ayerst), is claimed to be highly potent with minimal sedation as a side effect. Its dose level is low; namely, 4 mg. two to four times daily. It is also supplied in a sustained action tablet containing a total of 12 mg. under the name Theruhistin S.A. (Ayerst). These provide a fairly continuous therapeutic effect for 12 hours.

An antihistamine recommended particularly for use as an antipruritic agent is Sandostene (Sandoz). Chemically, it is methylaminophenyl-thenyl piperidine tartrate. It seems to have several mechanisms of action in addition to its antihistamine activity since it reduces capillary permeability and has an anticholinergic action. It is supplied in a 75 mg. sustained release tablet (Spacetab) and is indicated in pruritis, urticaria, drug reactions, and contact dermatitis.

Another new antihistamine is the product Dimetane (Robins). Chemically it is 1-(*p*-bromophenyl)-1-(2-pyridyl)-3-dimethylaminopropane maleate. It is claimed to have minimal side effects.

Anticholinergic Drugs

The search for the ideal anticholinergic drug to reduce gastrointestinal hypermotility and secretion continues. Many important and

useful drugs in this group are well known to the pharmacist. Some relatively new drugs in this category are the following:

Tricyclamol (Elorine—Lilly; Tricoloid—Burroughs Wellcome). This is a quaternary ammonium compound having the chemical name 1-cyclohexyl-1-phenyl-3-pyrrolidino-1-propanol. It is supplied as the sulfate or chloride. It provides relief in those conditions where spasm or hypermotility of the gastrointestinal tract is present such as peptic ulcer, pylorospasm, ileitis, and colitis. The dose ranges from 50 to 200 mg. three or four times daily.

Hexocyclium (Tral—Abbott). This is an anticholinergic drug particularly intended to relieve the hyperacidity and hypermotility in patients with peptic ulcer. The dose recommended is 25 mg. before each meal and at bedtime. It is contraindicated in patients with glaucoma and must be used with great care in patients having cardiac disease or prostatic hypertrophy.

Isopropamide Iodide (Darbid—S. K. F.). This new anticholinergic drug is (3-carbamoyl-3,3-diphenylpropyl) diisopropyl methyl ammonium iodide. Darbid is indicated in peptic ulcer, hyperchlorhydria, pylorospasm, spastic or irritable colon, and genitourinary spasm. It has a long duration of action; thus, the ending "bid" (twice a day). In combination with the tranquilizer Compazine, it is supplied as Combid Spansules (S. K. F.). This is a sustained release dosage form combining the calming effect of Compazine with the antispasmodic and antisecretory action of Darbid. Some patients require only one such capsule daily and the usual dose is only one every 12 hours.

Ataractic Drugs

So many new drugs have been introduced in this category that it has become necessary to classify them into several sub-groups. Thus, we have the potent tranquilizers such as chlorpromazine and reserpine; those having a calming action plus some muscle relaxant action such as meprobamate; ataractic drugs having a milder tranquilizing action than chlorpromazine; and, finally, some which seem to have an antiphobic action in that they control fear and tension.

The alkaloid rescinnamine is associated with reserpine in several Rauwolfia species including *Rauwolfia serpentina*. It is claimed to

produce fewer side effects than reserpine and to have therapeutic indications similar to those of reserpine. Thus, it is used in the treatment of tension and anxiety and also in hypertension. Rescinnamine is closely related to reserpine chemically, being a trimethoxycinnamyl reserpate, while reserpine is a trimethoxy benzoyl reserpate. It is available as Moderil (Pfizer) in 0.25 and 0.5 mg. tablets. Another Rauwolfia derivative is Deserpidine (Harmonyl—Abbott). It differs from reserpine in lacking a methoxy group on the indole ring structure. It is claimed to be more potent than reserpine and to cause much fewer side effects. It is given at about the same dosage level as reserpine and is available in 0.1, 0.25, and 1.0 mg. tablets.

A very potent new ataractic belonging to the phenothiazine group is Triflupromazine Hydrochloride (Vesprin-Squibb). This is 10-(3-dimethylaminopropyl)-2-trifluoromethyl-phenothiazine hydrochloride. It is claimed to be twice as potent as chlorpromazine. It is supplied as 10, 25 and 50 mg. tablets.

Prochlorperazine (Compazine—S. K. F.) is a tranquilizer of somewhat broader application than the more potent drugs like chlorpromazine (Thorazine—S. K. F.). It is used for mild to moderate emotional distress but is of less value in the more severe mental disorders. Compazine chemically is 2-cloro-10-[3-(1-methyl 4 piperazinyl) propyl]-phenothiazine. It is available in 5, 10, and 25 mg. tablets, in the sustained release capsule form known as the "Spansule", and in suppositories. The drug is also useful in controlling nausea and vomiting from such causes as gastroenteritis, radiation therapy, cancer, and pregnancy.

Another potent phenothiazine type ataractic is the drug Mepazine (Pacatal—Warner Chilcott). Chemically, it is 10-(N-methyl-3-piperidyl methyl) phenothiazine. It is useful not only in severe mental diseases but also as a general tranquilizer to potentiate analgesics, as preanesthetic medication, in nausea, chronic alcoholism, and drug withdrawal syndromes, etc. It has a selective action on the central nervous system without inhibiting the cortex and causing hypnosis. It is supplied as 25, 50, and 100 mg. tablets and in 2 cc. ampuls containing 25 mg./cc.

Another new, all-purpose tranquilizer is Perphenazine (Trilafon—Schering). This is 1-(2-hydroxyethyl)-4-[3-(2-chloro-10-phenothiazyl) propyl] piperazine. It is quite potent and the dose for simple tension states is only 2-4 mg. three times a day. Even the

most severe cases do not require more than 8-16 mg. two to four times daily.

Still another ataractic drug related to phenothiazine is thiopropazate dihydrochloride (Dartal-Searle). This is 1-(2-acetoxyethyl-4-[3-(2-chloro-10-phenothiazinyl) propyl]-piperazine dihydrochloride. It is supplied as 5 and 10 mg. tablets.

The drug Phenaglycodol (Ultran—Lilly) is 2-*p*-chlorophenyl-3-methyl-2, 3-butanediol. It has a calming action without producing hypnosis or euphoria and has a low toxicity so that it can be used safely for long periods. The dose is 300 mg. three or four times daily.

The psychotropic drug Benactyzine hydrochloride (Suavitil—Merck Sharp & Dohme) is a somewhat different acting drug than others classified as tranquilizers. It has been described as an "antiphobic" (removing worry and fear), an "anti-ruminant" (removing repetitious worrying), and a "mood normalizer". It is claimed to improve discrimination and learning and to improve precision of performance. Suavitil, chemically, is 2-diethylaminoethyl benzilate hydrochloride. It is claimed that this drug is superior to other ataractics in depression states since most others worsen the depression. Suavitil in contrast eliminates fear and produces a mild anti-depressant action. It is supplied as 1 mg. tablets.

Psychic Stimulants

The use of drugs such as amphetamine, methamphetamine, Pipradol (Meratran—Merrell), and methyl phenidyl acetate (Ritalin—Ciba) to elevate the mood and overcome depression is a common practice with the physician.

The drug Phenmetrazine hydrochloride (Preludin—Geigy) is especially recommended as a central stimulant to assist the patient in dieting (anorexiant). Chemically, it is 2-phenyl-3-methyl-tetrahydro-1, 4-oxazine hydrochloride. It is available as 25 mg. tablets.

In using isoniazid (isonicotinyl hydrazide) as an adjuvant with streptomycin in the treatment of tuberculosis, its mood elevating effect is a common side reaction and one which often produces a misleading subjective improvement. The isopropyl derivative of isoniazid is an even more potent stimulant without an anorexiant action such as is produced by amphetamine. This isopropyl derivative, Iproniazid (Marsilid—Hoffmann LaRoche) is useful in treating severe depression in psychiatric patients as well as in ambulatory patients. It

seems to act by inhibiting amine-oxidase which affects the metabolism of serotonin and other amines involved in brain function.

Marsilid is also of value in treating depressed patients with chronic disability or illness causing improvement in well being and appetite. The drug often requires some time before its effect is noticeable—often as much as two weeks. The dosage must also be carefully adjusted so as to avoid overstimulation and excitement in the patient. The dose ranges from 50 to 100 mg. daily with the maximum being 150 mg. per day. It is contraindicated in epilepsy, in patients taking meperidine, and those with impaired kidney function.

Diuretics

The importance of potent diuretics in correcting the edema so frequently associated with cardiovascular disease is well known. In recent years, some excellent new mercurial diuretics have been developed including some of the thiol type having low tissue toxicity. Non-mercurial diuretics have also been developed such as the carbonic anhydrase inhibitor Diamox (Lederle). Others have been Mictine (Searle) and the drug replacing it Rolicton (Searle).

A new carbonic anhydrase inhibitor is the product Ethoxzolamide (Cardrase-Upjohn). Chemically, it is 6-ethoxybenzothiazole-2-sulfonamide. Like Diamox (Lederle), it is used in congestive heart disease, glaucoma, and the edemas of pregnancy and the premenstrual period. It is supplied as 125 mg. tablets.

The latest diuretic from early reports appears to be almost ideally suited for use in the control of edema. It is known as chlorothiazide (Diuril—Merck Sharp & Dohme). Diuril is 6-chloro-7-sulfamyl-1, 2, 4-benzo-thiadiazine-1, 1-dioxide. Diuril is a carbonic anhydrase inhibitor but it enhances the secretion of *both* sodium and chloride by the kidney tubules. Potassium is also excreted but to a lesser extent and bicarbonate loss is negligible. Diuril is well absorbed following oral administration and the drug does not lose its effectiveness even after long use. The fact that both sodium and chloride ions are excreted together prevents the acidosis sometimes observed with other carbonic anhydrase inhibitors. Diuril will even reverse the salt retention observed with adrenal steroids such as cortisone.

Diuril is used in the edema of congestive heart disease, renal edema such as that associated with nephrosis and nephritis, hepatic

edema, premenstrual tension caused by fluid retention, drug induced edema, and the edema of obesity. It also appears to be very useful in the treatment of certain types of hypertension.

The usual dose is one or two 0.5 Gm. tablets once or twice a day. Care must be taken to observe the patient for electrolyte and fluid imbalance such as hypokalemia. This, although rare, would be serious particularly in patients on digitalis therapy.

Biliary Abstergent

A new hydrocholeretic and biliary abstergent is available which appears quite promising. It is known as Florantyrone (Zanchol—Searle). This new substance is not a steroid and, therefore, not chemically related to cholic acid or its derivatives. Zanchol chemically is γ-oxo-γ (fluoranthene) butyric acid. It causes marked changes in the quantity and quality of bile when administered to patients. The volume and fluidity are increased, the color improves—changing to green, sediment and bacteria diminish, and the bile foams more on shaking. All of these indicate improved functioning by the liver parenchyma.

Zanchol is of value in chronic cholecystitis, for post-cholecystectomy patients with T-tube drainage, and for the prevention and treatment of post-cholecystectomy syndrome. It is, of course, like all hydrocholeretics, contraindicated in biliary tract obstruction and other conditions where stimulation of the liver cells is not desirable.

Zanchol is available in the form of 250 mg. tablets and the dose is 3 or 4 daily.

Adrenal Steroids

The development of water-soluble adrenal steroid derivatives for topical use in ophthalmic and dermatologic products is of interest. One such product is prednisolone 21-phosphate used as its monosodium salt. The solubility of this prednisolone compound is about 2000 times that of the parent compound and it should provide better penetration into inflamed tissue. In the eye, it avoids the use of suspended particles as when the steroids themselves are employed.

This new product is known as Hydeltrasol (Merck Sharp & Dohme). It is available in the form of a topical lotion, an ophthalmic solution, and an ointment—all containing 0.5 per cent of the soluble steroid—and also as a 0.25 per cent ophthalmic ointment. Combined

with the antibiotic neomycin sulfate, it is supplied as a topical lotion, an ophthalmic solution, and a nasal spray under the name Neo-Hydeltrasol (Merck Sharp & Dohme).

Hydrocortisone diethylaminoacetate supplied as Magnacort (Pfizer) is claimed to be unique in that its partition coefficient favoring water over fat causes it to penetrate skin lesions more readily than hydrocortisone but to be poorly absorbed into the deeper fatty tissues and thence into the blood. This increases its local efficiency and diminishes its systemic effect. It is available as a 0.5 per cent ointment and also in combination with neomycin sulfate as Neo-Magnacort Ointment (Pfizer).

The improvement in the clinical usefulness of cortisone by the introduction of a double bond in the Δ_1 position (prednisone) has led to intensive studies to develop new modifications having greater efficiency and fewer side effects. A new steroid recently introduced is 6-methyl-Δ_1-hydrocortisone (Medrol—Upjohn). This differs from prednisolone only in the presence of a methyl group at position 6. Medrol is somewhat more effective than prednisolone and it is also claimed to cause even less sodium and fluid retention, almost completely eliminating the hazard of edema. It also appears to cause less epigastric distress and psychic stimulation. It is supplied as 4 mg. tablets.

The problem of sodium and water retention as a side effect of adrenal steroid therapy was greatly reduced with the advent of the Δ_1 unsaturated steroids, prednisone and prednisolone. The 6-methyl derivative of prednisolone appears even better in this respect but there still remains the problem of nitrogen loss through protein catabolism, and increased gastro-intestinal motility and secretion. Some recently announced experimental steroids offer some promise of improvement by still further reducing these side effects. American Cyanamid (Lederle) has reported on a new derivative, Triamcinolone Aristocort (Lederle), Kenacort (Squibb). This is 16-hydroxy-9-α-fluoroprednisolone. Another improved steroid announced by E. R. Squibb is 21-fluoro-9-α-fluoroprednisolone which by animal experiments appears to be 10-15 times as potent as hydrocortisone in its glucocorticoid and anti-inflammatory action but with little or no action causing sodium and water retention. Clinical trials on these latter two are in progress to establish their relative value in therapy.

Another announcement of interest is the potentiation of adrenal steroids by the introduction of a methyl group at position 2. For

example, 2-methyl-hydrocortisone is much more potent in both its glucocorticoid and mineralocorticoid activity than hydrocortisone, and 2-methyl-9-α-fluorohydrocortisone is more potent than aldosterone. The latter (aldosterone), isolated from an extract of the adrenal gland is believed to be the most potent naturally occurring mineralocorticoid and many more times more potent than desoxycorticosterone.

Sex Steroids

The enhancement in potency of the natural adrenal steroids by some changes in their structure is also seen in the field of the sex hormones. A very potent new androgen is Fluoxymesterone (Halotestin—Upjohn). This is the 9-α-fluoro-11-β-hydroxy derivative of methyltestosterone. Halotestin is about 5 times as potent as methyltestosterone. It is supplied in 2 and 5 mg. tablets and is used orally.

A new long acting testosterone ester is testosterone enanthate (Delatestryl—Squibb). Enanthic acid is *n*-heptanoic acid so that this new ester is similar to the propionate except in having a seven carbon acid esterified with the alcohol group at position 17 on the steroid instead of a three carbon acid. Delatestryl is very long-acting since a single intramuscular injection of this drug in oil provides a therapeutic effect for 2-4 weeks. It is supplied in an injectable form containing 200 mg./cc. Combined with estradiol valerate, it is supplied as Deladumone (Squibb). This is a long-acting estrogen-androgen combination for use in treating the menopausal syndrome and osteoporosis. It contains 90 mg. of testosterone enanthate and 4 mg. of estradiol valerate per cc. and the dose is 1-2 cc. every 2-4 weeks.

Some new steroids having very potent progestational activity are Norethindrone (Norlutin—Parke Davis) and Norethynodrel (Searle). Norlutin is 17-α-ethinyl-19-nor-testosterone. It differs from Ethisterone U. S. P. only in that it lacks a methyl group at position 19; thus, the term 19-nor. Norlutin is recommended wherever potent progestin therapy is indicated such as threatened abortion. It is supplied as 5 mg. tablets and the dose is 5-10 mg. twice a day.

Norethynodrel is 17-α-ethinyl-17-hydroxy-5(10)-estraene-3-one. It differs from Norlutin only in having a double bond between carbons 5 and 10 rather than 4 and 5. It is supplied only in combination with the 3-methyl ether of ethinylestradiol under the name Enovid (Searle). Enovid is a potent progestin with some little estrogenic

action by reason of the presence of the ethinylestradiol ether. It is useful in metrorrhagia, menorrhagia, primary and secondary amenorrhea, dysmenorrhea, and premenstrual tension. The dosage schedule and particularly the period of dosage during the menstrual cycle must be regulated according to the condition being treated. For example, if ovulation is to be suppressed, therapy should begin on day 5 of the cycle; whereas, if ovulation is desired, therapy should be during the period, day 15 to day 25. There is good evidence that continued dosage with Enovid results in anovulatory cycles by reason of its suppression of pituitary gonadotropins but it is not recommended as a contraceptive drug. Enovid is supplied in tablet form each containing 10 mg. of the progestin and 0.15 mg. of the associated estrogen.

The progestin, 17-α-hydroxyprogesterone-17-n-caproate (Delalutin—Squibb), is a long-acting product for intramuscular use. It is supplied in vials containing 2 and 5 cc. containing 125 mg./cc. A single intramuscular injection provides a sustained action for about 2 weeks. As the acetate, this same steroid is used orally having about twice the activity of Ethisterone. It is available as Prodix (Upjohn).

Anabolic Steroid

The anabolic (body-building) effect of androgens is a well-known therapeutic application of such drugs. Their masculinizing effect, however, is a serious handicap. A number of related steroids having an anabolic effect but with minimal androgenic activity have been developed including methyl androstene-diol. The latest steroid in this category is norethandrolone (Nilevar—Searle) which is 17-α-ethyl-17-hydroxynorandrosterone. It differs from methyl testosterone in having an ethyl group instead of a methyl on C number 17 and lacking a methyl at position 19. Nilevar is used to create positive nitrogen balance in recovery from prolonged illness, in wasting diseases, in premature infants, malnutrition, etc. It is available in 10 mg. tablets and the adult dose is 30-50 mg. daily. Like the androgens, it should not be given in prostatic carcinoma and must be used with great care when there is evidence of liver damage.

Anti-Infectives

Before discussing some of the newer antibiotics, it would seem advisable to describe some of the important developments among the well-established agents in this class. The superior qualities of

penicillin V (phenoxymethyl penicillin) in resisting acid destruction in the stomach has led to its very extensive use as the oral penicillin of choice. It has been used as the acid form but recently its potassium salt was shown to be more rapidly absorbed when given orally and superior to the acid form. Therapeutic blood levels are reached within 15 minutes after oral administration and maximum levels attainable are twice those of the acid form and four times those of penicillin G. The potassium penicillin V is supplied as V-Cillin-K by Eli Lilly in 125 and 250 mg. tablets, equivalent to 200,000 and 400,000 units.

The well-known penicillin splitting action of the enzyme penicillinase can give rapid relief in penicillin reactions. For this purpose it is available as Neutrapen (Schenley).

A new soluble form of Chloromycetin (Parke Davis) is the sodium acid succinate. This water-soluble salt has one of the carboxyls of succinic acid esterified with an alcohol group of Chloromycetin while the other has its acidic hydrogen replaced by sodium. It can be given intravenously and intramuscularly in aqueous solution and it is superior to the older injectable forms. It is also useful topically such as in aerosolized form for respiratory infections.

The use of tetracyclines in the form of their phosphate complex or in combination with sodium metaphosphate gives evidence of superiority over the chloride. Blood levels are claimed to be almost double those attained using the chloride. The phosphate is believed to bind certain ions in the gastro-intestinal tract that interfere with the absorption of the tetracycline. The phosphate complex or combination is available as Panmycin Phosphate (Upjohn), Sumycin (Squibb), Tetracyn V (Pfizer), and Tetrex (Bristol) in several dosage forms. A citric acid-oxytetracycline combination having similar advantages is supplied as Achromycin V (Lederle). The combination of the antifungal antibiotic nystatin (Mycostatin) with a tetracycline first introduced as Mysteclin (Squibb) is now also available as Achrostatin (Lederle) and Comycin (Upjohn).

The combination of tetracycline and oleandomycin introduced as Sigmamycin (Pfizer) is being altered using a phosphate buffered tetracycline and oleandomycin as the phosphate to improve absorption and give higher blood levels. The new product replacing Sigmamycin is known as Signemycin V (Pfizer).

A new derivative of oleandomycin, triacetyloleandomycin, was recently reported as giving higher blood and urine levels than the

non-acetylated form and combinations of oleandomycin and neomycin have been reported as quite effective in reducing the bacterial flora of the intestine prior to surgery.

An entirely new antibiotic substance Ristocetin (Spontin—Abbott) was recently released. Ristocetin is composed of two related compounds, ristocetin A and B, which are isolated from the fermentation medium of a new species of Actinomycetes, *Nocardia lurida*. Both ristocetin A and B are large molecules with a molecular weight of about 4000. They are stable in acid solution, less stable at a neutral pH, and inactivated by alkali. As Spontin (Abbott), they are supplied as a lyophilized mixture administered intravenously after being dissolved in 5 per cent dextrose solution. It cannot be used orally or by other parenteral routes since, when in contact with tissue, it is irritating.

Ristocetin is effective against staphylococci and enterococci including many strains resistant to other antibiotics. Clinically, it has proven life-saving in many cases where patients were dying with an infection resistant to all other therapy. It appears to be much more active *in vivo* than indicated by *in vitro* tests and gamma globulin also enhances its activity. Ristocetin unlike many antibiotics is bactericidal rather than simply bacteriostatic.

In pneumococcal and streptococcal infections, a dosage of 25 mg./Kg. per day is usually adequate. In staphylococcal infections, up to 50 mg./Kg. per day may be needed. In endocarditis due to resistant strains, dosages as high as 75 mg./Kg. per day may be needed. The daily dose is administered in 2 or 3 divided amounts at regular intervals and treatment should be continued 2 or 3 days after clinical response, and for even longer at a lower dose (1 Gm./day) in endocarditis. The drug is administered by intravenous drip in 5 per cent dextrose with the maximum concentration used being 1.25 per cent and the maximum rate of administration for this concentration 2 cc. per minute.

Side effects include dermatitis, diarrhea, occasional thrombophlebitis proximal to the injection site, and occasional depression of white cell count with a relative neutropenia. The life-saving qualities of this new drug, however, seem to justify its use in spite of possible side effects. The patient must, of course, be kept under careful check to note any developing signs of toxicity.

A number of new antibiotic substances were reported at the fourth annual Antibiotics Symposium held in Washington, D. C. in

October 1957. Among these, in addition to ristocetin, were PA 132, nucleocidin and alazopeptin. Pfizer scientists described a new group of antibiotics named the quinocycline complex and also a number of new antifungal agents known as PA 150, PA 153, and PA 166.

The Japanese drug, Kanamycin, is being produced in the U. S. by Bristol Laboratories and is now under clinical test. It has been reported effective against the tubercle bacillus, staphylococci, and *S. typhosus* and to be less toxic than streptomycin.

Sulfonamides

The sulfonamide, sulfaethylthiadiazole, was introduced in the United States last year as Sul-Spansion (Smith, Kline & French). It is a suspension of sustained release pellets providing prolonged therapeutic blood levels. Each 5 cc. contains 0.65 Gm. of sulfaethylthiadiazole. The dose for adults is 15 cc. every 12 hours with the initial dose twice this amount. For children under 75 lb. (34 Kg.), the dose should be about 2.5 cc. per 15 lb. body weight. Sulfaethylthiadiazole is a very soluble sulfonamide both in free and acetylated form. Only a small per cent is acetylated by the body leaving it in free and active form. It is rapidly absorbed and also has rapid renal clearance. In sustained release form, the rapid absorption and renal clearance permits it to be used without frequent doses and large variations in blood levels.

A second sustained release form of this drug recently introduced is Sul-Spantab (Smith, Kline and French). These contain 0.65 Gm. in pellet form; i.e., the same amount as present in 1 teaspoonful (5 cc.) of the Sul-Spansion liquid. The dosage schedule is the same as that described, each tablet being equal to 5 cc. of the liquid suspension.

Sulfaethylthiadiazole has an antibacterial spectrum similar to other sulfonamides but it is rarely accompanied by side effects or signs of toxicity. It is, of course, contraindicated in patients known to have impaired kidney function or sensitivity to sulfonamides.

Another new sulfonamide is sulfamethoxypyridazine (Kynex—Lederle; Midicel—Parke-Davis). This chemically is 3-sulfanilamido-6-methoxypyridazine. While it is a very soluble sulfonamide, it is very slowly excreted. For example, a single dose of 2 Gm. will maintain therapeutic blood levels for 72 hours while with most other sulfonamides a similar dose would provide effective levels for only 6 hours. This property permits lower dosage and less frequent administration.

Kynex is particularly recommended for urinary infections but, since it passes the blood brain barrier well, it is also useful in meningitis. The concentration in the cerebrospinal fluid is about 50 per cent that in the blood. The drug is also used for other generalized infections caused by sulfonamide sensitive organisms. Its utility as a prophylactic in preventing recurrent streptococcic infections in rheumatic fever patients has also been established and a dose of only 30 mg./Kg./week appears to be adequate.

Kynex is supplied as 0.5 Gm. tablets and as a syrup containing 0.25 Gm./5 cc. The adult dose is 2 Gm. initially, followed by 0.5-1.0 Gm. after 12 hours and daily thereafter.

The usual precautions taken with sulfonamide therapy should be followed such as attention to possible blood dyscrasias and checking kidney function.

Miscellaneous Anti-Infectives

Two new products for treating vaginitis are Sterisil (Warner-Chilcott) and Tricofuron (Eaton Laboratories). Sterisil is supplied as a gel in individual dosage cylinders. It contains as its active ingredient hexetidine (bis-1,3(β-ethylhexyl)-5-methyl-5-amino-hexahydropyrimidine). This is said to be effective against bacteria, monilia, and trichomonads.

Tricofuron, available in both suppository and powder form, contains Furoxone (Eaton) which is N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone and Micofur (Eaton) which is *anti*-5-nitro-2-furaldoxime. The former is a potent trichomonacide and the latter a fungicide. Thus, this combination is effective against the two most common causes of vaginitis; namely, *Trichomonas vaginalis* and *Monilia albicans.*

The well-known property of polyvinyl pyrrolidone (PVP) to complex with various substances has been utilized in preparing various topical products containing iodine and supplied under the name Isodine (Isodine Pharm. Corp.). Iodine when complexed with PVP loses much of its tissue irritating action and toxicity but still retains some of its antiseptic action. A solution, an ointment, and a medicated foot powder containing this iodine-PVP complex are available.

Short-chain free fatty acids are well-known fungicides and products containing propionic, caprylic, and other organic acids and their salts have long been used for this purpose. A new and interest-

ing approach in treating fungus infections of the skin is seen in the product Enzactin Cream (Ayerst). This contains as its active ingredient 25 per cent glyceryl triacetate. Its mechanism of action depends on its hydrolysis under the influence of esterases found on the skin and elaborated by fungi and other organisms. On hydrolysis, free acetic acid is formed which acts both to restore the pH of the skin to normal and also retard the growth of the fungi. This mechanism is self-regulating since the liberated acid also retards esterase activity until the pH again rises whence more glyceryl triacetate is hydrolyzed and more acid formed.

The use of adsorbent clays combined with antibacterial agents in the treatment of diarrheas is a standard form of therapy and many such products are marketed. A new preparation believed to be a markedly superior anti-diarrheal product is Polymagma (Wyeth). This is a pectin and alumina gel suspension containing Claysorb (Wyeth), which is an activated attapulgite, dihydrostreptomycin sulfate, and polymyxin B sulfate.

The activated attapulgite which it contains has been shown by laboratory studies to be several times as effective as the best grades of kaolin in adsorbing bacteria and bacterial toxins. The combination of antibiotics used exerts a synergistic effect against a number of bacteria known to be involved in many intestinal infections leading to diarrhea. Polymagma is available in 8 fluidounce (240 cc.) bottles and the dose for adults is 20 cc. 3 or 4 times a day taken before meals.

A new potent tuberculostatic drug has been announced. It is Pyrazinoic acid amide (Pyrazinamide—Merck Sharp & Dohme). It is a white crystalline substance, soluble in water, and available as 0.5 Gm. tablets. At the present time, it is distributed only through hospitals. Pyrazinamide is intended for the short term protection of gravely ill patients when other drugs cannot be used or are ineffective. When combined with isoniazid, the combination is believed to be the most potent tuberculostatic therapy known. It is particularly useful in preparing patients for chest surgery and as continuing therapy through a 6-8 week postoperative period.

The daily dose (divided doses) is up to but not exceeding 35 mg./Kg.

The drug Quinacrine Hydrochloride (Atabrine—Winthrop) has many and varied uses other than its action as an antimalarial. Thus, it has been reported of value as an anthelmintic and even in rheumatoid arthritis. Its latest reported use is in infectious mononucleosis

where it appears to give excellent results. The dose is 0.1 Gm. 4 times daily.

Another antimalarial drug found useful in the treatment of an unrelated condition is the 4-aminoquinoline derivative Plaquenil Sulfate (Winthrop). In the treatment of chronic discoid lupus erythematosus and polymorphic light eruptions, it appears to be superior to both quinacrine and chloroquine also used for these conditions.

Biologicals

In the field of biologicals, much attention was given in 1957 to the program for the development of a monovalent vaccine for the new Asian strain of influenza. As production meets demand, the trend is to supplant the monovalent vaccine with a polyvalent product containing this new strain in addition to the several others known to cause influenza outbreaks.

It has also been possible to double the potency of the monovalent vaccine increasing it to 400 chick cell agglutination units (CCA-units) per ml. This increases its prophylactic efficiency.

The acute respiratory and conjunctival infections caused by adenoviruses has been given considerable attention in recent years. These viruses are also called the APC viruses (adenoidal, pharyngeal, conjunctival) and they cause considerable illness and absenteeism in schools and industry. A prophylactic vaccine against this acute respiratory infection is now available as Adenovirus Vaccine (Parke-Davis). It gives protection against types 3, 4, and 7 of the virus. The dose is 1 cc. intramuscularly.

The treatment given those exposed to rabies was originally developed by Pasteur. While such an antirabies vaccine is fairly effective, it has frequently caused serious paralytic complications in the patient, sometimes resulting in death. A new rabies vaccine is now available with the virus having been grown on duck embryo tissue. After growth, the virus is killed by the addition of β-propiolactone which is a potent virucidal agent. It is completely free of the paralytic factor, the hazard present in vaccine prepared by growing the virus on the brain tissue of rabbits. The vaccine is injected subcutaneously once each day for 14 days and is used to prevent rabies in exposed persons. In this connection, it should be remembered that one need not be bitten by a rabid animal to contract rabies.

Inoculation with the saliva through a cut or abrasion is all that is required. The extent of exposure and the location of the inoculation site is of great importance. If a person is bitten around the face or neck, it is probably advisable to use a rabies antiserum for passive immunization and protection until the use of rabies vaccine can give an active immunity.

New Nitrogen Mustard

A new potent anti-leukemia drug related to the nitrogen mustards is the drug Chlorambucil (Leukeran—Burroughs Wellcome). Chemically, it is *p*-(di-2-chlorethyl) aminophenylbutyric acid. It is indicated in the treatment of chronic lymphocytic leukemia, malignant lymphomas, and Hodgkin's disease. Like all such drugs, it produces only a remission of the disease and is not curative. Leukeran, however, does not seem as toxic to the hematopoietic system as other drugs in this class. It is available as a 2 mg. tablet. Dosage schedules and precautions must be read and followed by the physician very carefully for this very potent drug as with all anti-leukemia agents.

Endocrines

It is now believed that thyroxine is altered in the body forming *l*-triiodothyronine which is the substance directly responsible for the regulation of cellular metabolic activity. The substance *l*-triiodothyronine was first isolated from thyroid extract using paper chromatography. It is now made in quite pure form synthetically. It is known as Liothyronine and supplied as Cytomel (Smith, Kline & French). The racemic form (dl) is sold as Trionine (Roche). Triiodothyronine has a much more rapid onset of action than thyroid or thyroxine and a shorter duration of action. This permits better control of its dosage and action. It is used for the same therapeutic purposes as powdered thyroid or thyroxin.

The principle behind "lente" insulin is the precipitation of zinc insulin in an acetate buffer in a manner to carefully control its particle size. This new type of repository insulin avoids the use of proteins such as globin and protamine; yet, it provides a long-acting effect on injection. Lente Insulin as originally supplied in the U. S. (Lente Iletin—Lilly) was very similar in onset and duration of action to NPH insulin (Isophane Insulin Injection U.S.P.). The Danish workers originating "lente" insulins prepared several types differing

in particle size and, therefore, in duration of action. In fact, by admixing different particle sizes, the onset and duration of action can be very nicely controlled.

Two new "lente" insulins released in the U. S. by Lilly are the Semi-Lente Iletin and the Ultra-Lente Iletin. The former contains smaller particles than Lente and has a duration of action less than Lente, being only 12-16 hours. Ultra-Lente is made up of larger particles and has a duration of action of 36 hours or longer. All are supplied in 10 cc. vials containing 40 or 80 units/cc.

While not an endocrine, the use of sulfonylureas orally in the control of diabetes mellitus deserves comment here. The drug, Carbutamide, was withdrawn from clinical trial in 1957 because of toxic effects which were reported. A very close relative, Tolbutamide (Orinase—Upjohn), did not show similar toxicity and after extensive clinical trials was released for prescription use. It is interesting to note that the only difference in structure between the toxic Carbutamide and the drug Tolbutamide is that the former has an amino group on the benzene ring while, in the case of Tolbutamide, it is replaced by a methyl group.

Tolbutamide (Orinase—Upjohn) is 1-butyl-3-*p*-tolylsulfonylurea. It is available as 0.5 Gm. tablets. It has given evidence of being useful in selected cases of diabetes. For example, it will control blood sugar when taken orally in most diabetics who contracted the disease when adults. In children, it is rarely or never of value. This, it is believed, is because it depends for its action on the presence of some functioning beta cells in the pancreas which are capable of secreting insulin. Current belief is that the drug stimulates the beta cells to greater insulin production. Even in adults, if the diabetes is severe and requires more than 40 units of insulin a day, Orinase is not likely to be effective. In many cases, however, it can be used in place of insulin and some authorities believe over half of all diabetics could use it with success. The dose must be regulated according to the patient's needs. The maximum, when beginning therapy, is 3 Gm. daily and the maintenance dose varies from 0.5 to 1.5 Gm. daily.

The synthesis of both vasopressin and oxytocin, the two hormones of posterior pituitary, was announced by DuVigneaud only a short time ago. Synthetic pure oxytocin is now available as Syntocinon (Sandoz). It has the advantage over the natural product isolated from posterior pituitary that it is completely free of foreign protein and contains none of the associated principle vasopressin. It is

supplied in 1 cc. ampuls containing 10 international units and 0.5 cc. ampuls containing 5 units.

Blood Modifiers

A new injectable iron preparation that appears to be quite superior to most others is one consisting of a Dextran-Iron complex. It is supplied as Imferon (Lakeside). Each cc. supplies the equivalent of 50 mg. of elemental iron and the product is injected intramuscularly. In making the intramuscular injection, the upper skin layers should be pulled laterally before inserting the needle. This prevents staining the subcutaneous tissue which might be somewhat permanent should it occur. This new product avoids the necessity of the intravenous route required by some iron preparations such as those containing saccharated iron oxide.

Calculation of a patient's iron needs can be made based on the hemoglobin per cent and a course of therapy instituted to assure this amount being made available. Imferon is supplied in 2 and 5 cc. ampuls.

Two new anticoagulant drugs are Acenocoumarin (Dipaxin-Upjohn) and Sintrom (Geigy). Dipaxin is 2-diphenylacetyl-1, 3-indandione. Its action is one of long duration similar to that of bishydroxycoumarin. It is supplied as 1 mg. and 5 mg. tablets. Sintrom is 3-(α-acetonyl-4-nitro-benzyl)-4-hydroxycoumarin. Sintrom has an intermediate duration of action lying between that of bishydroxycoumarin and Tromexan (Geigy). Its action can be reversed in 24-48 hours by cessation of therapy. Sintrom is supplied as 4 mg. tablets.

Anticoagulant therapy once employed largely as a prophylactic procedure following surgery to prevent thromboembolism is now widely employed in selected cases of congestive heart failure, cardiac vascular surgery, coronary thrombosis, thrombophlebitis, and other conditions where the hazard of a thromboembolism exists.

A drug combination to prevent and control bleeding is the preparation Adrestat (Orginon). This contains adrenochrome semicarbazone (as the salicylate), sodium menadiol diphosphate, hesperidin, and vitamin C. This combination is for oral use; whereas, Adrestat (F) is an injection product containing only adrenochrome semicarbazone (as the salicylate).

The oral product is available in lozenge and capsule form.

Prior to and after surgery, the oral product is used for several days. This is accompanied by the use of the injection product just before surgery.

The adrenochrome semicarbazone is said to act by causing the retraction of severed capillary ends and making them less fragile to trauma. The function of the other components of the oral product is to stimulate prothrombin formation and correct capillary fragility.

Unsaturated Fatty Acids

Very extensive research has been conducted in the past few years on the effect of diet on blood cholesterol levels and the incidence of atherosclerosis. Considerable evidence points to the role of saturated fats (animal) as contributing to hypercholesterolemia and atherosclerosis when they are consumed in sizable amounts. On the contrary, unsaturated fats such as found in certain vegetable and fish oils seem to have a protective action beyond that which might be expected just by substituting them for animal fats. The protective action is believed to be contributed by the unsaturated fatty acids present in the constituent glycerides. The mechanism of their action, as postulated by some workers, is that, when present in the lipoprotein complex containing the cholesterol, the unsaturated fatty acids improve its mobility and transport thus retarding its deposition in the intima of blood vessels and the formation of an atheromatous plaque.

A number of products containing unsaturated fats have been released recently for use in hypercholesterolemia associated with atherosclerosis or where it is believed to suggest the possible development of atherosclerosis. One of these products is Linodoxine (Pfizer) which is available both in capsules and as an emulsion. This contains safflower oil, a rich source of unsaturated fatty acids, and pyridoxine hydrochloride. The latter is claimed by some to be involved in the conversion of linoleic acid to the protective fatty acid arachidonic.

Another similar product is Arcofac (Armour) which is also supplied as an emulsion. The product Saff (Abbott) is also an emulsion of safflower oil.

Lufa Capsules (U.S. Vitamin) in addition to safflower oil and pyridoxine contains the lipotropic factors methionine, inositol, and choline bitartrate.

Lenic Capsules (Crookes-Barnes) is another such product and is also supplied with 100 mg. of niacin. The latter (niacin), in large

doses, has also been reported as having a blood cholesterol reducing action.

More products in this category are certain to be developed and promoted, particularly if clinical experience with those now available shows them to be useful.

Diagnostic Aids

Sodium radio-iodide is now available as a finished pharmaceutical for both diagnostic procedures and therapy. The use of I^{131} as a means of determining basal metabolic rate is claimed to be much more accurate than the usual method. For such a diagnostic procedure two forms are available: Radiocaps (Abbott) and Tracervial (Abbott). The former are empty gelatin capsules with carrier-free sodium radio-iodide adsorbed on the inner walls. On successive weeks, they are made in different colors to help the user distinguish different lots. Using one capsule as the standard, another is administered to the patient and the per cent taken up by the thyroid measured after a stated time interval. For example, hyperthyroid patients will have over 50 per cent taken up by the thyroid at 24 hours and hypothyroids less than 10 per cent. The diagnostic dose given is 5-50 μc. For those preferring a liquid product, the Tracervial can be used. This is a solution containing on the day of calibration 25 μc of activity/cc. For therapeutic use in thyrotoxicosis (toxic goiter) and thyroid neoplasms, a sterile solution for injection is supplied (Sterile Sol. Therap.—Abbott), an oral solution (Oriodide—Abbott), and capsules (Theriodide—Abbott). The dose, of course, must be very carefully estimated and measured taking into account the age in days of the product and its decay rate. Care must also be taken to protect all personnel handling the therapeutic material.

A new method to determine the acid secretory function of the stomach eliminates the need for the use of a gastric tube to obtain gastric fluid. The test utilizes the Diagnex Blue Unit (Squibb). In this test, gastric secretion is stimulated by the administration of caffeine sodium benzoate on a fasting stomach. One hour later, the Diagnex Blue granules are given suspended in ¼ glass of water. These contain azure A dye adsorbed on an exchange resin. In the stomach, the blue dye is released by acid, hydrogen ions being exchanged for the dye. The dye is then excreted in the urine where it can be measured by visual comparison with color standards.

A new organic iodine preparation for intravenous urography is sodium and methylglucamine diacetylamino triiodobenzoates (Renografin—Squibb). Renografin is reported to give excellent opacifications after 10-15 minutes following the intravenous injection of 20 ml. of the solution. A 1 ml. test dose is supplied in the package to test the patient for sensitivity. This is standard practice for all such organic iodine preparations to be given intravenously.

APPLIED INTERPROFESSIONAL RELATIONS IN PHARMACY *

By T. A. Nooner, Sr.**

AT no time in the history of pharmacy has the need for Applied Interprofessional Relations approached its present importance. Today, regardless of which branch or specialty of pharmacy one is practicing, he finds himself forced into still closer working relations with the members of the professions allied with his own. He is, therefore, required to apply his knowledge of interprofessional relations as ardently and as seriously as he does any of the other basic subjects he studied while in a school of pharmacy. How well he does this may easily determine his success or limitation. This requirement comes from without as well as within his own profession. The ever-growing interest and attention now being given to both interprofessional and public relations, plus the constantly increasing number of pharmacists who now make a determined effort to meet these demands, are convincing evidences of the importance of Applied Interprofessional Relations to pharmacy and to ourselves as individual pharmacists.

Let us take a brief view of one or two basic reasons that make the practice of interprofessional relations of such importance to pharmacy. Our profession and we as individual pharmacists are of first consideration. If pharmacy is to be maintained and respected as an honored profession, then we, its members, must be so possessed of this conviction that we radiate it in our daily practices. In other words, we must live it. This fact is substantiated by one of nature's time-proven laws; namely, one cannot convey something to another he does not possess. Every conscientious and sincere pharmacist holds his profession in high regard. He desires to see it so recognized and respected by all. This is why we all but despair when we hear and see how lightly the professional standing of pharmacy is regarded by some of the public and even by some of our own members. This could not be if all within our ranks had lived and upheld our code of

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ethics and the silent vows every true pharmacist pledges within himself when he enters the profession. We, the pharmacists of today, must recognize and accept the changes that have been and are taking place in pharmaceutical and medical circles. These are of such force and magnitude that they can no longer be looked upon with complacency. They require action that will keep our profession in line to meet present day requirements. For example, compounding, the strong support that upheld our professional recognition for generations, has had to give way to other responsibilities that, when properly applied, afford even stronger support to our professional standing. Once the challenge these new and greater obligations and responsibilities present is realized and accepted, the more and greater opportunities we shall have to make pharmacy the profession we all want it to be. We have no choice but to face these requirements and work earnestly and unceasingly to bring the public into the full realization that present day pharmacy does indeed merit its full confidence and respect as an honored profession. No doubt we all share the conviction that the members of our allied professions will gladly support our cause once they realize the sincerity of our purpose. We certainly cannot go forward without their endorsement and support. This is one of the prime reasons why Applied Interprofessional Relations means so much to us today. Once we have co-professional relations wholeheartedly practiced and enjoyed, the members of other health professions and the public will be quick to realize that we are indeed an active member of the professional team which constantly labors in behalf of the health welfare of all.

The public is another reason for our being diligent in the practice of interprofessional relations. Let us remember a profession cannot exist unless it is a public necessity. Therefore, we readily see why it is so important that the public be kept aware of how these new and improved changes in medical and pharmaceutical circles affect the professional status of pharmacy. In Applied Interprofessional Relations we deal directly with the members of our allied professions. They meet the public under favorable circumstances and conditions to influence its opinions. For example, the public frequently seeks the physician's advice regarding the pharmacist and generally his directions and recommendations are accepted without question. Where the physician regards the pharmacist as a co-professional, he carries his conviction to his patients. We cannot think of a better

or more effective approach to win the respect and good will of others for pharmacy than through the spoken word of a highly respected physician. There are timely ways within our grasp as individuals and as a profession to bring them to a fuller realization of how necessary pharmacy is to the health welfare of all.

As a profession we have our standards; our code of ethics and the oath of Maimonides. But how many of the public have even heard of them. Is it not discouraging to see how few within our own ranks recognize their significance and worth? To bring the import of all of this still closer to home, I need only to remind you of but one expression we have all heard. "There is no longer a need for even a four-year course in pharmacy for one to be able to fill the prescriptions of today. All one needs is to be able to read, count, pour and write or type correctly." There are far too many people who feel this way, or they say they do. Such false and damaging expressions are heard too often. As much as we regret to say it, these expressions are in no wise limited to the lay public, occasionally one comes from a member of an allied profession and, yes, even from the thoughtless within our own ranks. Does not this fault lie within ourselves and is it not enough to arouse us to seek effective means to offset such misleading impressions? They put us on the defensive, a position we cannot tolerate. Here Applied Interprofessional Relations is a forceful medium to convert these negative expressions into positive opinions and good will.

May we view our subject as it pertains to the different branches or specialties of pharmacy. Since the vast majority of us practice retail pharmacy, let us look at some of the things Applied Interprofessional Relations means to those within this group. The retail pharmacist's field is so wide that he should have a broad knowledge of all subjects pertinent to pharmacy including interprofessional relations. In retail pharmacy one has the choice of a highly commercial store, a well-balanced commercial and professional pharmacy or a highly professional pharmacy. Regardless of which he elects to enter, he quickly finds the need for a good knowledge of interprofessional relations as he will have many opportunities to apply it to his advantage.

Many pharmacists devote much, if not all, of their time to the practice of interprofessional relations. It is here we meet the branch or specialty of pharmacy which was well-named "Medical Service

Pharmacy" by our committee on Professional Terminology in '52. We shall deal with this a bit later. As we study the needs of present day pharmacy, we readily see how completely wrong are the impressions that pharmacy has become a trade and professional training is no longer necessary. We see no reason to question the fact that the progress being made in both medicine and pharmacy places us in a new position; one that will bring pharmacy and medicine still closer together if we do our part in welding this relationship. The pharmacist needs to broaden his knowledge of drugs and their actions. He needs to have a more fundamental understanding of pharmacology, chemistry, etc.; likewise, he needs to broaden his knowledge of anatomy, especially that of the nervous, circulatory, digestive, respiratory systems, etc. Also a good understanding of interprofessional relations and how to apply it is of special importance to him. This alone justifies enlarging and extending the curricula of our schools of pharmacy. Such knowledge is essential if the pharmacist is to properly impart the information the members of our allied professions are asking of us today. The pharmacist who is so qualified imparts correct and dependable information on the more complex and potent medicinals and does so with complete assurance of its accuracy and clarity. He is secure in his statements because he knows what he is talking about. The physicians and others he serves look upon him as a learned and trusted co-professional. This pharmacist also realizes he is neither a diagnostician nor physician. He keeps within his own profession and has the confidence and respect of all. Through his ability to serve, he becomes a necessity to the members of his allied professions as well as his own. He is proud to be known as a pharmacist and does much to heighten the professional level of pharmacy.

The retail pharmacist we are discussing keeps abreast with the developments in his profession. He also makes good use of a part of the time he formerly gave to compounding by reading and studying the journals of his allied professions, thus he is familiar with their progress. He is well versed in interprofessional and public relations and knows how to apply this knowledge effectively and appreciatively. He is tactful, thus is able to convert what might otherwise be an affront into a gratuity. He builds respect and good will; knows the dangers of being placed on the defensive and how to present his viewpoint in a manner that gains confidence and respect. This pharmacist never violates a professional confidence nor does he quote anyone unless he has their permission to do so or their views have

been expressed in print. He watches his terminology and upholds his profession at all times. He often converts a disparaging opinion of pharmacy into one of appreciation and praise. Rather than wait for an opportunity to develop, he creates his own. He applies interprofessional relations effectively and those he serves respect pharmacy for the profession it is.

The hospital pharmacist has much in common with the retail pharmacist who gives recognition to the professional phase of pharmacy. Those who practice this specialty do much to further and maintain our professional standard. The pharmacy is usually located within or adjacent to the hospital, thus, the pharmacist is in close touch with the staff physicians and especially the resident physicians, internes, externes, registered nurses, etc. This affords him more frequent visits by those in medicine and nursing and more opportunities and reasons to apply interprofessional relations in his practice. The demands upon his professional knowledge are wide indeed. They may range from answering a simple question for an externe to clearing a scientific point on a complex medicinal chemical for a leading internist. He often helps the young physician to understand the basic principles of a well-written prescription; that is, to see he is thoroughly familiar with the abbreviations, characters, terminology, directions, dosage, etc. In carrying out these aids he establishes himself as a worthy co-professional, one who is a source of dependable information. All of this means he is forced to draw upon his knowledge of interprofessional relations with as much consideration as he does the other basic subjects taught in our schools of pharmacy. Let us not overlook how time-lasting his work is with these young physicians and how ever ready they are to lend their support to our cause.

Let us now look at a branch or specialty of pharmacy which in my opinion has long deserved more recognition and support than it has received—Medical Service Pharmacy. It is practiced to some degree by every pharmacist regardless of which branch or specialty he follows. Medical Service Pharmacy is as important to a small pharmacy as it is to a large one. However, due to the volume of business, many of our larger pharmacies have a key pharmacist who gives much if not all of his time to this phase of the work. There is another and larger group who give it full attention. These pharmacists represent pharmaceutical and medicinal chemical manufacturers. Their work forces them to continually draw upon their professional knowledge, thus they have many opportunities to further the cause of pharmacy.

May we take a closer look at the potential of the Medical Service Pharmacists, one who represents a local pharmacy and one a pharmaceutical manufacturer. These men interview six or more physicians a day plus their work with other pharmacists, dentists, doctors of veterinary medicine and registered nurses. They also interview the faculty members of schools of medicine, dentistry, pharmacy, veterinary medicine, etc. The scope of their work is broad. No one in pharmacy is called upon more often for professional information and I know of none who has more opportunities to further the welfare of pharmacy than these ever-active and loyal Medical Service Pharmacists. They are constantly in touch with those who are in strategic positions to acquaint those they serve with what pharmacy means to the health welfare of all. Their daily lives are filled with opportunities to gain respect and good will for our profession because the opinions and recommendations of those they serve are accepted with appreciation and confidence.

At times a Medical Service Pharmacist may labor under disturbing if not disheartening conditions. Among the underlying causes are so few people know and understand his work and even some of those with whom he works are prone at times to discredit his contribution to medicine and pharmacy. Too many who represent pharmaceutical houses, unfortunately, have little knowledge of drugs and their actions. Representatives of this group have caused some physicians to feel that all who call on them are not qualified to discuss a complex medicinal. Since the Medical Service Pharmacist has had professional training and knows how to apply interprofessional relations effectively, he quickly dispels such opinion when given an opportunity. As we consider this particular point, let us ask ourselves if any pharmacy would employ someone who is not a pharmacist to represent its interest among the physicians and other members of the health professions. The answer is obvious. It shows us clearly why pharmacists and physicians alike prefer a pharmacist to give them information on a new and potent drug and clarify points on older ones. Such preference has been voiced by many physicians as the late W. A. Bastedo (1), whose memory we respect and honor; William Hildebrand (2), past president of the American Academy of General Practice; W. H. Anderson (3), Editor of THE MISSISSIPPI DOCTOR; J. P. Sanders (4), past president of the American Academy of General Practice, and many others. It is our earnest hope that a standard will be established whereby all who assume the duties of a

Medical Service Pharmacist will be required to meet the same educational qualifications. This would fulfill a duty and an obligation of our profession to all of its members and the public it serves. Once this group has such endorsement and support of our profession, its schools; and national, state and local associations, it will become a driving force of solidified and determined effort that will make pharmacy more attractive to our young folk and raise it to a higher professional level. Where else can we find a group of comparable strength and action that would work as a unit to present our cause to the physicians and other members of our allied professions? These members of the health professions are our intermediaries to the public. Their influence reaches far and lasts long. I know of none that can offer comparable influence to gain and hold the respect and good will of the public for pharmacy. The prime source of this influence stems from the efforts of the Medical Service Pharmacist who applies interprofessional relations with forethought and a purpose.

The student of pharmacy merits our fullest consideration in this study. In him lies the future of our profession and it is such a short time until he will be in full control of its status. It is, therefore, our conviction that we shall be most unfair to the student of pharmacy unless the curricula of our schools of pharmacy are adjusted and extended to present day requirements. All subjects that afford the best and strongest support to the professional status of pharmacy must be included. We have no choice but to make pharmacy so attractive to our young people that it will have a strong appeal to the honor student. Talk is not enough but conviction, supported by action that will adjust the practical and scientific subjects in the curricula to the needs of today, will give the prospective applicant an attractive picture, the student security in his professional hopes and we pharmacists a great deal more professional pride and satisfaction.

As stated before this Section at the Boston meeting in '54, it has been my privilege to observe and study the reaction of the senior student to a course on Interprofessional Relations, one in which he received full credits. I repeat, the close attention and keen interest he gave throughout the 34 one-hour lectures were indeed most gratifying. The course was designed to awaken the student to the full realization that he would be a full-fledged co-professional with the physician and others upon his graduation and registration. Likewise, to help him better appreciate the knowledge gained in his other subjects and to realize knowledge is of little or no value until it is

imparted and shared with others. The student was shown how to apply Interprofessional Relations through personal demonstration and as a result he became more interested and gained confidence and security in himself. A course in Interprofessional Relations must be broad, so much so that it requires far more time than has yet been given to the subject. Only careful study and experience will determine the time this course should have. Let us give our students every consideration that they may be equal to the demands of the present and future pharmacy—a profession appreciated by all.

Now to the group that holds the keys to the approach and the solution of our problem—our schools of pharmacy and the members of their faculties. Their position within the profession and regarding existing conditions are such that we look to them for help and guidance as well as leadership. Many of our leaders realize the necessity of enlarging and extending the curricula in our schools of pharmacy and that Interprofessional Relations is a subject of prime importance. In fact, we are indeed heartened at the attention and interest being given to courses on Interprofessional Relations and other subjects that promise to keep pharmacy abreast with the progress being made by our allied professions. There are good indications that more of our colleges of pharmacy are awaking to these needs and some show every indication of including such subjects in their curricula. Could the members of the faculties of our schools share even a day or so with a pharmacist of each branch or specialty of pharmacy, they too would be amazed at the number and types of questions he is asked. They would also be astonished to note how deep they go into the scientific phases of pharmacy and how pleased the interviewed is to have the information. I give you these thoughts as some in our schools have but limited opportunity to observe the pharmacist of the different branches or specialties in action. May I urge you to make it a point to study the work of these pharmacists more closely and observe how effectively they apply interprofessional relations to the welfare of our cause. I am confident that once the importance of interprofessional relations is realized it will become a fully accredited subject in your curricula.

As we look to the future of pharmacy, let us ponder well the needs for Applied Interprofessional Relations in Pharmacy. May we view it as the strong support it is that upholds our professional standing; one that helps us meet the necessities of today and fulfills our hopes for tomorrow.

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SELECTED ABSTRACTS

Aminitrozole in Oral Therapy of Trichomonas Vaginitis. Barnes, J., Boutwood, A., Haines, E., Lewington, W., Lister, E., and Haram, B. J. *Brit. Med. J.* No. 5028:1160 (1957). A group of 37 patients with trichomonas vaginitis were treated by the oral administration of 100 mg. aminitrozole (2-acetylamino-5-nitrothiazole) 3 times a day for 10 days. A buffered vaginal jelly with a pH of 4 and containing acetic acid, boric acid, oxyquinoline sulfate, ricinoleic acid, and glycerin in a vegetable gum base (Aci-jel) was administered intravaginally night and morning for 3 weeks. Control patients, initially 21 in number, were treated with the vaginal jelly only on the same schedule. Vaginal smears were taken at the first visit and then after 2, 4 and 6 weeks. Control cases which were positive after 4 weeks were transferred to the treated group.

Altogether, 6 of the 37 patients treated were cured of trichomonas infestation. Twenty of the patients had one course of treatment, 10 had two courses, and 7 had three courses. Four of the patients cured had but one course of therapy. None of the control patients became negative without treatment.

The husbands of eight of the patients were examined and two were found to be positive for trichomonads. Both of these became negative following treatment with aminitrozole.

The authors also studied the diagnostic value of culturing the swab from the vaginal secretions in the simplified trypticase serum medium of Kupferberg. It was found that fewer cultures were found to be positive than initial hanging drop specimens. Therefore, they concluded that a careful examination of a hanging drop preparation was more dependable for diagnostic purposes than the culture technique.

With regard to oral therapy with aminitrozole and topical treatment with vaginal jelly, the authors concluded that results did not warrant further use of the treatment.

The Absorption of Sulfonamides From Lipid and Aqueous Preparations. Daeschner, C. W., Bell, W. R., Stivrins, P. C., Yow, E. M., and Townsend, E. *A. M. A. J. Dis. Children 95:370* (1957). The absorption, following the oral administration of a single dose of acetyl sulfisoxazole, sulfadiazine and a triple sulfonamide in the form of a lipid emulsion and as an aqueous suspension, was evaluated by the blood levels attained in a series of infants and children.

When acetyl sulfisoxazole was administered in a lipid emulsion, free sulfonamide was found in the blood after one hour, it reached a peak after two hours, and remained high through an eight-hour period. Following a similar dose as an equeous suspension, the level after one hour was approximately one-half that obtained from the lipid emulsion. A peak level less than that from the lipid product was reached after four hours. When a normal diet, including milk, was given following the administration of the aqueous suspension, the blood level was somewhat higher than that of fasting children but still less than that obtained from the lipid emulsion.

When sulfadiazine was administered, the peak from both types of preparations was reached in about four hours but the level from the acqueous suspension was about one-half that from the lipid emulsion. When food, including milk, was given following the aqueous suspension, a peak blood level was attained after about six hours with a sustained level that was higher than that from the lipid emulsion after eight hours and twenty-four hours.

The administration of the triple sulfonamide produced a peak blood level after about four hours from both preparations. However, the aqueous suspension provided a level about 20 per cent lower than that from the lipid emulsion.

Considering an optimum dosage schedule, the authors concluded that a 12 hour interval between doses of the lipid emulsion form of acetyl sulfisoxazole should provide an effective therapeutic regimen.

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